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(n = 70) were asked to state their preferences between two health improvements, each with different starting points and magnitude of change, until the point of indifference was found. The Wilcoxon signed rank test was used to determine the statistical significance of the differences between health changes that were of equal value to the respondent. **RESULTS:** In Experiment I, where utilities were represented to participants using a visual analogue scale, all ten comparisons showed that if two health improvements are of equal magnitude, individuals will place a greater benefit valuation upon the improvement that has a more severe initial health state. This evidence was largely reflected in Experiment II, which used the Health Utilities Index: Mark 3 multi-attribute function to represent utilities using a descriptive method. In Experiment II, eight of the ten comparisons suggested that this was the case. **CONCLUSION:** Using experimental techniques, this study was able to show that 'equal' health improvements were valued more, when the initial health state was more severe. Furthermore, a method was developed in order to quantify the effect of starting disease severity, and to develop a 'modified QALY gain' measure for use in economic evaluation.

PMC18

THE ROLE OF CONCEPTUAL MODELS, ENDPOINT MODELS, AND CONCEPTUAL FRAMEWORKS WHEN MAKING TREATMENT BENEFIT CLAIMS TO THE FDA

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OBJECTIVES: Conceptual models, endpoint models, and conceptual frameworks are research tools used by patient reported outcome (PRO) researchers. The objective of this study was to understand and clarify the role of each tool and to understand the relationships between them in relation to making treatment benefit claims to the FDA. **METHODS:** Published literature and expert consultation were used to explore definitions, development strategies, and use of each tool. **RESULTS:** A conceptual model is a representation of proposed causal linkages among a set of concepts. It can be developed from reviewing the literature, and interviewing patients and clinicians. An endpoint model is a representation of the relationships between all measures that may be defined as endpoints (primary or supportive) in a clinical trial. It is developed from a systematic/comprehensive review of disease literature and/or a conceptual model, the Target Product Profile (TPP), clinical experts, and the clinical development team. A conceptual framework is a representation of the expected relationships of items within a domain and of domains within a PRO concept. It is developed during the development of a PRO and is validated during the process of psychometric validation. Each of these tools fit together to take researchers from early drug development through to eventual treatment benefit claim. **CONCLUSION:** Each of the models discussed are useful research tools and the endpoint model and conceptual frameworks are essential for treatment benefit claims to be made to the FDA. They can be easily differentiated and their interrelationships within the timescale of the drug development and treatment benefit claim process can be modelled.

PMC19

USE OF THE RELIABLE CHANGE INDEX TO EVALUATE CLINICAL SIGNIFICANCE IN HEART TRANSPLANTS

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OBJECTIVES: A current challenge for clinicians is to know when functional health outcomes are clinically meaningful, and we have used the Reliable Change Index (RCI) with the most widely used self-report measure of functional health (the SF-36) for determine it. The aim was to determine a clinically significant change in SF-36 outcomes from pre-to-post-heart transplant. **METHODS:** A total of 150 patients from eleven transplant hospitals in Spain were included in the waiting list and 80 of them received a heart transplant and were prospectively studied. Subjective evaluation of HRQoL over time (before and at 12 months postransplantation) was obtained using the Short Form-36 (SF-36). The differences between pre and postrasplant were calculated for the clinical records and correlated with the differences on HRQoL. A standardization of the SF-36 scores was applied. Two criteria to determine clinical significance by the RCI:1) the pre-post difference score exceeds the RCI and 2) post-transplant score fall within the range of normative values. **RESULTS:** Comparing the individual domains of SF-36 showed significant improvement pre and postransplantation. The correlation between differences in clinical and HRQoL variables showed that, as large was the difference in NYHA functional Class, the greater was the improvement on PCS; and as greater was the improvement on PCS, the younger was the patient. First and second criterion for clinical significance were satisfied: 1)Patients had average changes in SF-36 scores that exceeded the RCI in all dimensions except for bodily pain dimension, and 2)All postransplantation scores were in the normal range (between 45 and 55) except Social Functioning dimension. **CONCLUSION:** Patients perceive heart transplant as capable of improving their HRQoL and were clinical significant except for Bodily Pain and Social Functioning. While the notion of clinical significance is not clearly defined in HRQoL studies, the RCI method is a usefull strategy for identifying clinically meaningful SF-36 outcomes.

PMC20

UTILITY WEIGHTED COMPARED TO UNWEIGHTED EQ-5D AND HUI3 SUMMARY SCORES: IMPLICATIONS FOR STATISTICAL INFERENCE

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OBJECTIVES: As utility-based health measures, the EQ-5D and HUI3 draw from a different theoretical basis than psychometrically-derived measures, yet both weighted utilities and unweighted approaches find common application as outcomes in clinical trials where inferential statistics are applied. The objective of this study was to compare the statistical properties of the EQ-5D and HUI3 health state classifier systems using weighted utility scores (WUS)to using unweighted simple summary scores (SSS). **METHODS:** WUS and SSS were calculated for EQ-5D and Health Utilities Index Mark 3 (HUI3) health state classifier systems using two longitudinal datasets (n(stroke) = 124; n(rehabilitation) = 264). Validity was evaluated using F-statistics from ANOVA-based known groups comparisons. Pre/post paired t-tests were used to evaluate responsiveness. The relative efficiency (RE) ratio of for each of the statistics was calculated between WUS and SSS, with differences outside the range of 0.8 to 1.25 (e.g. >25%) interpreted as substantial. **RESULTS:** Greater statistical power was associated with WUS groups than SSS in known groups comparisons for EQ-5D (50% of RE > 1; no substantial differences) and HUI3 (100% of RE > 1; 75% substantial). WUS tended to be more responsive for the HUI3 (62.5% of RE > 1; 37.5% substantial), while SSS